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Amendment and Response

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Serial No.: 10/788,731

Confirmation No.: 6098

Filed: 27 February 2004

For: SELECTIVE MODULATION OF TLR-MEDIATED BIOLOGICAL ACTIVITY

Amendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1. (Previously Presented) A method of identifying a compound that selectively modulates at least one TLR-mediated cellular activity, the method comprising:

providing an assay to detect modulation of a TLR7-mediated cellular activity and an assay to detect modulation of a TLR8-mediated cellular activity;

performing the assay to detect modulation of a TLR7-mediated cellular activity using a test compound and human cells that naturally express TLR7;

performing the assay to detect modulation of a TLR8-mediated cellular activity using the test compound and human cells that naturally express TLR8; and

identifying the test compound as a compound that selectively modulates at least one TLR-mediated cellular activity if the test compound modulates the TLR7-mediated cellular activity to a different extent than it modulates the TLR8-mediated cellular activity.

2. (Previously Presented) The method of claim 1 wherein the compound modulates a TLR7-mediated cellular activity and does not modulate a TLR8-mediated cellular activity.

3. (Previously Presented) The method of claim 1 wherein the compound modulates a TLR8-mediated cellular activity and does not modulate a TLR7-mediated cellular activity.

4-8. (Canceled)

9. (Currently Amended) A method of identifying a target compound having a TLR modulation profile that conforms to a target TLR modulation profile, the method comprising:

selecting a target TLR modulation profile;

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- determining the TLR modulation profile of a test compound by:
- providing an assay to detect modulation of a first TLR-mediated cellular activity and an assay to detect modulation of a second TLR-mediated cellular activity,
 - performing the assay to detect modulation of the first TLR-mediated cellular activity using the test compound,
 - performing the assay to detect modulation of the second TLR-mediated cellular activity using the test compound, and
 - determining the extent to which the test compound modulates each TLR-mediated cellular activity; and
- identifying the test compound as a target compound if the TLR modulation profile of the test compound conforms to the target TLR modulation profile.
10. (Original) The method of claim 9 wherein at least one TLR modulation profile comprises TLR6-mediated cellular activity.
11. (Original) The method of claim 10 wherein at least one TLR modulation profile comprises modulation of TLR6-mediated cellular activity.
12. (Original) The method of claim 11 wherein at least one TLR modulation profile comprises substantially no modulation of TLR7-mediated cellular activity.
13. (Original) The method of claim 9 wherein at least one TLR modulation profile comprises TLR7-mediated cellular activity.
14. (Original) The method of claim 13 wherein at least one TLR modulation profile comprises modulation of TLR7-mediated cellular activity.

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15. (Original) The method of claim 14 wherein at least one TLR modulation profile comprises substantially no modulation of TLR6-mediated cellular activity.
16. (Original) The method of claim 14 wherein at least one TLR modulation profile comprises substantially no modulation of TLR8-mediated cellular activity.
17. (Original) The method of claim 9 wherein at least one TLR modulation profile comprises TLR8-mediated cellular activity.
18. (Original) The method of claim 17 wherein at least one TLR modulation profile comprises modulation of TLR8-mediated cellular activity.
19. (Original) The method of claim 18 wherein at least one TLR modulation profile comprises substantially no modulation of TLR7-mediated cellular activity.
20. (Original) The method of claim 9 wherein at least one TLR modulation profile comprises TLR9-mediated cellular activity.
21. (Original) The method of claim 20 wherein at least one TLR modulation profile comprises modulation of TLR9-mediated cellular activity.
22. (Original) The method of claim 9 wherein the target TLR modulation profile includes one or more TLR-mediated cellular activities that are not detectably modulated by a target compound.
- 23-24. (Canceled)

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25. (Previously Presented) A method of selectively modulating cells of the immune system, the method comprising:

identifying a first human immune system cell population that naturally expresses TLR7 and a second human immune system cell population that naturally expresses TLR8;

selecting a compound that modulates a TLR7-mediated cellular activity of the first cell population to a different extent than it modulates a TLR8-mediated cellular activity of the second cell population; and

contacting cells of the immune system with the selected compound in an amount effective to modulate a TLR-mediated cellular activity of at least one of the cell populations.

26. (Original) The method of claim 25 wherein the method further comprises determining the TLR expression profile of the first cell population and the TLR expression profile of the second cell population.

27. (Original) The method of claim 26 wherein the step of selecting a compound comprises comparing the TLR expression profile of the first cell population and the TLR expression profile of the second cell population with a TLR modulation profile of the compound.

28. (Original) The method of claim 25 wherein modulating cells of the immune system comprises detectably activating the cells or detectably inhibiting the cells.

29. (Original) The method of claim 25 wherein the compound modulates the first cell population and does not detectably modulate the second cell population.

30. (Original) The method of claim 25 wherein the compound modulates both cell populations.

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31. (Original) The method of claim 25 at least one cell population is modulated *in vitro*.
32. (Original) The method of claim 25 wherein at least one cell population is modulated *in vivo*.
33. (Original) The method of claim 25 wherein at least one immune system cell population comprises plasmacytoid dendritic cells.
34. (Previously Presented) The method of claim 25 wherein at least one immune system cell population comprises monocyte-derived dendritic cells.
- 35-55. (Canceled)
56. (Previously Presented) The method of claim 25 wherein the compound modulates the second cell population and does not detectably modulate the first cell population.